Please note:

If you experience some difficulty in viewing some of the pages, use the magnifying tool to enlarge the specific section

EVIDENCE THAT *GSTT1* AFFECTS THE INDUCTION OF GLYCOPHORIN A VARIANT CELLS IN SMOKERS R.G. Langlois[1], A.M. Lockhart[2*], M.A. Watson[2*], C.L. Thompson[2*], and D.A. Bell[2*] [1]Lawrence Livermore Natl. Lab., Livermore, CA; [2]NIEHS, RTP, NC.

Human risks from environmental or occupational chemical exposures may be affected by genetic variations in metabolic enzymes responsible for activating and detoxifying these agents. We hypothesized that polymorphisms in metabolism could modulate somatic mutation among individuals exposed to tobacco smoke. We analyzed variant frequency (VF) at the glycophorin A (GPA) loci for 23 non-smokers and 50 smokers (16-90 cigarettes per day) and tested to see if polymorphisms in glutathione S-transferase genes (*GSTM1* and *GSTT1*),or N-acetyltransferase genes (*NAT1* and *NAT2*) affected GPA VFs in these groups. Among nonsmokers we observed no significant genotype effects on GPA NØ or GPA NN VF. In smokers, no significant differences in mean GPA VF were observed for *GSTM1*, *NAT1* and *NAT2* genotypes, but the *GSTT1* null genotype was associated with a significant higher NN VF among smokers. Ethylene oxide, a mutagenic component of cigarette smoke and a substrate for GST Theta 1, has been shown to form hemoglobin adducts in erythrocytes of smokers. Among the metabolism genes tested, only *GSTT1* is highly expressed in the erythrocyte cell lineage. Thus, the *GSTT1* null genotype, which results in an absence of GST Theta 1 enzyme in erythrocytes, may be a genetic risk factor for elevated tobacco smoke-induced GPA mutation. [Work performed under the auspices of the U.S. Department of Energy by LLNL under contract W-7405-ENG-48 and Interagency agreement Y01-ES-80171 (NIEHS)]